| Substitute Form PTO 1390 U.S. Departme |   |  |  |   |  |  |  |  |
|--|---|--|--|---|--|--|--|--|
|  |   |  | O THE UNITED STATES                          | 50304/114001                              |  |  |  |  |
|  |   |  | ) OFFICE (DO/EO/US)<br>UNDER 35 U.S.C. § 371 | U.S. Application Number:                  |  |  |  |  |
|  |   | FILING   | UNDER 35 0.3.C. § 37 1                       | Not yet assigned                          |  |  |  |  |
| INTERNATIONAL APPLICATION NUMBER       |   |  | INTERNATIONAL FILING DATE                    | PRIORITY DATE CLAIMED                     |  |  |  |  |
| PCT/EP2004/010198                      |   |  | September 13, 2004                           | September 12, 2003                        |  |  |  |  |
| TITLE OF INVENTION:                    |   | PTERIDINE DERIVATIVES FOR THE TREATMENT OF SEPTIC SHOCK AND $TNF\text{-}\alpha\text{-}$ RELATED DISEASES |  |   |  |  |  |  |
| APPLICANTS FOR DO/EO/US:               |   | Mark Jozef Albert WAER, Piet André Maurits Maria HERDEWIJN, Steven Cesar Alfons                          |  |   |  |  |  |  |
|  |   | DE JONGHE, Arnaud Didier Marie MARCHAND, Lin YUAN, Sefrioui EL HASSANE                                   |  |   |  |  |  |  |
| Appli                                  | cant herewith submits to the U  | nited States   | s Designated/Elected Office (DO/EO/US)       | the following items and other information |  |  |  |  |
| 1.                                     | This is a FIRST submission of items concerning a filing under 35 U.S.C. § 371.  |  |  |   |  |  |  |  |
| 2.                                     | □ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. § 371.   |  |  |   |  |  |  |  |
| 3.                                     | ☑ This is an express request to begin national examination procedures (35 U.S.C. § 371(f)).   |  |  |   |  |  |  |  |
| 4.                                     | ☑ The U.S. has been elected.  |  |  |   |  |  |  |  |
| 5.                                     | <ul> <li>A copy of the International Application (35 U.S.C. § 371(c)(2)).</li> <li>∞ a. is transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>∞ b. has been transmitted by the International Bureau.</li> <li>□ c. Is not required, as the application was filed with the United States Receiving Office (RO/US).</li> </ul> |  |  |   |  |  |  |  |
| 6.                                     | An English language translation of the International Application into English (35 U.S.C. § 371(c)(2)).  |  |  |   |  |  |  |  |
|  | □ a. is transmitted herewith.<br>□ b. has been previously submitted under 35 U.S.C. 154(d)(4).  |  |  |   |  |  |  |  |
| 7.                                     | Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. § 371(c)(3)).   |  |  |   |  |  |  |  |
|  | <ul> <li>a. are transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. have been transmitted by the International Bureau.</li> <li>c. have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>I d. have not been made and will not be made.</li> </ul>                               |  |  |   |  |  |  |  |
| 8.                                     | □ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. § 371(c)(3)).   |  |  |   |  |  |  |  |
| 9.                                     | ☑ An oath or declaration of the inventors (35 U.S.C. § 371(c)(4)). (2 pages)  |  |  |   |  |  |  |  |
| 10.                                    | □ An English language translation of the annexes to the International Preliminary Examination Report under PCT Articl 36 (35 U.S.C. §371 (c)(5).  |  |  |   |  |  |  |  |
| 11.                                    | □ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98.   |  |  |   |  |  |  |  |
| 12.                                    | □ An assignment for recording. A separate cover sheet in compliance with 37 C.F.R. §§ 3.28 and 3.31 is included.  |  |  |   |  |  |  |  |
| 13.                                    | ☑ A preliminary amendment.  |  |  |   |  |  |  |  |
| 14.                                    | □ A substitute specification.   |  |  |   |  |  |  |  |
| 15.                                    | □ A power of attorney and/o   | r change of  | f address letter.                            |   |  |  |  |  |
| 16.                                    | Request for Deferred Exa  | mination.  |  | <u></u>                                   |  |  |  |  |
| 17.                                    | Application Data Sheet.   |  |  |   |  |  |  |  |
| 18.                                    | Other items or information: Request (7 pp.); Demand (5 pp.); Notification (1 p.); IPRP (17 pp.); and WO/2005 00255 A2 (79 pp.)  |  |  |   |  |  |  |  |

| 19.   | wing fees are subr  | nitted:   |  |  |                        |           |
|---|---|---|--|--|------------------------|-----------|
| Basic National Sta  | age Fee: \$300  | \$300.00  |  |  |                        |           |
| National Stage Se   | arch Fee  | \$500.00  | -  |  |                        |           |
|   |   |   | en paid on the interna<br>al Search Authority: \$1   |  |                        |           |
| International Sear  | ch Report prepared  | and p   | rovided to the Office:   | 6400   |                        |           |
| All other situations  | s: \$500  |   |  |  |                        |           |
| National Stage Ex   | amination Fee   |   |  |  | \$200.00               |           |
| satisfied provision   | s of PCT Articles 3   | on repo<br>3(1)-(4)                                   | ort prepared by USPTC<br>): \$100  | ) and all claims   |                        |           |
| All other situations  |   |   |  |  |                        |           |
|   | ) for furnishing the c<br>d priority date (37 C   |   | declaration later than § 1.492(e)).  | 30 months from   | \$0.00                 |           |
| CLAIMS  | NUMBER FI   | ED  | NUMBER EXTRA   | RATE   |                        |           |
| Total claims  | 20-20 =0  |   | 0  | x \$50   | \$0.00                 |           |
| Independent clain   | ns 1 - 3 =0   |   |  | x \$200  | \$0.00                 |           |
| Multiple depender   | nt claims (if applicat  | ole)  |  | + \$360  | \$0.00                 |           |
| 100 sheets (exclu   | ding sequence listir  | ig or co  | cification and drawings<br>omputer program listin<br>ch additional 50 sheets   | g filed in an  |                        |           |
| TOTAL SHEETS  | EXTRA SHEETS  | a<br>fr   | lumber of each<br>dditional 50 sheets or<br>action thereof (round<br>p to a whole number)  | RATE   |                        |           |
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|   |   | 1   | TOTAL OF ABOVE CA  | LCULATIONS =   | \$ 1,000               |           |
| Reduction of 1/2 f<br>entity status under   | or filing by small en<br>37 C.F.R. § 1.27.  | tity, if a  | applicable. Applicant c  | laims small  | \$500.00               |           |
|   |   |   |  | SUBTOTAL =   | \$500.00               |           |
|   |   |   | English translation lat<br>e (37 C.F.R. § 1.492(f  |  | \$                     |           |
|   |   |   | TOTAL N  | ATIONAL FEE =  | \$                     |           |
|   | nied by an appropri   |   | (37 C.F.R. 1.21(h)). T<br>ver sheet (37 C.F.R. §   |  | \$                     |           |
| -   |   |   |  | TOTAL FEES =   | \$500.00               |           |
|   |   |   |  |  | Amount to be refunded  | \$        |
|   |   |   |  |  | charged                | \$ 500.00 |
| <ul> <li>□ b. Please charg</li> <li>∞ c. The Commiss<br/>overpayment</li> <li>NOTE: Where an</li> <li>1.137(a) or (b) mu</li> </ul> | e my Deposit Accou<br>ioner is hereby auth<br>to Deposit Accoun<br>appropriate time lim | int No.<br>horized<br>t No. 0<br>hit unde<br>ted to i | the above fees is enc<br>03-2095 in the amound<br>to charge any additio<br>03-2095.<br>er 37 C.F.R. §§ 1.494 of<br>restore the application | nt of [**] to cover the second s | y be required, or crea |           |
| James D. DeCam<br>Clark & Elbing LLF<br>101 Federal Stree   | P Fac   | the   | and the second                           |  |                        |           |